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Rooney

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(54) **METHODS AND COMPOSITIONS FOR REGULATING THE INTRAVASCULAR FLOW AND OXYGENATING ACTIVITY OF HEMOGLOBIN IN A HUMAN OR ANIMAL SUBJECT**

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(*) Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Under 35 U.S.C. 154(b), the term of this patent shall be extended for 0 days.

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Related U.S. Application Data

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(52) **U.S. Cl.** **514/6**; 514/832; 514/833; 530/385; 530/402

(58) **Field of Search** 514/6, 832, 833; 530/385; 604/7; 423/374, 405; 424/608

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(57) **ABSTRACT**

Methods for time-regulated prophylaxis or treatment of animals or humans for limited circulatory oxygen delivery induced by the inhibitory effects of a plasma-borne hemoglobin-based material on L-arginine→nitric oxide→cGMP pathways in the arteriovenous vasculature. The properties of the invention restore and increase circulatory oxygen delivery by increasing circulatory flow of the blood-hemoglobin-based material through selective activation of L-arginine→nitric oxide→cGMP pathways in the arterial rather than venous vasculature. A method of the invention utilizes oxygen-carrying biocolloid compositions that consist of a hemoglobin-based material and a guanosine 3':5'-cyclic monophosphate (cGMP) generating entity, for treatment of animals and humans in need thereof for diseases or medical conditions which utilize the biocolloids as hemodiluents, blood substitutes, plasma expanders, or resuscitative fluids. The invention provides selective administration of cGMP generating entities for prophylaxis or treatment of animals or humans with limited circulatory oxygen delivery induced by a plasma hemoglobin-based material arising from intravenous administration, disease or medical condition. Most importantly, the invention provides for time-controlled enablement of the oxygen-deliverying properties of the invention that would be used for treatment of specific diseases or medical conditions requiring time-dependent increases in circulatory oxygen delivery.

30 Claims, 14 Drawing Sheets